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An Efficient, Stable and Reusable Palladium Nanocatalyst: Chemoselective Reduction of Aldehydes with Molecular Hydrogen in Water

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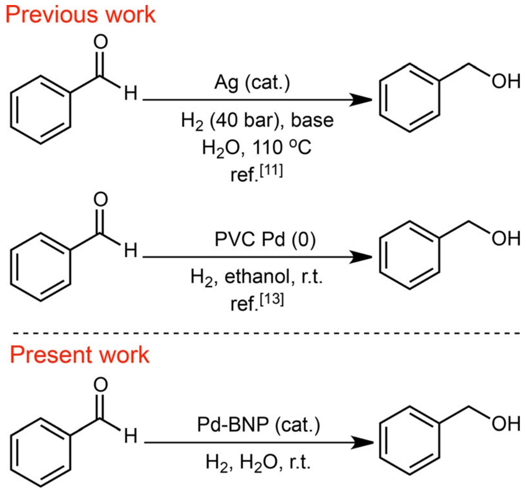
Abstract: Palladium nanoparticles (Pd-BNP) stabilized by a binaphthyl-backbone can be efficiently used for the chemoselective reduction of aldehydes in the presence of hydrogen at room temperature in water. The Pd-BNP catalyst is easily recovered and reused for five catalytic cycles.

Keywords: aldehydes; binaphthyl-stabilized palladium nanocatalyst; chemoselective reduction; reusable catalyst; water as a solvent

Hydrogenation of functional groups is an indispensable reaction in synthetic chemistry and the reduction of functional groups such as carbonyl groups, nitro groups, C-C and C-hetero atom multiple bond plays a major role for the synthesis of numerous biologically important molecules, natural products, and drugs.[1,2] Common methods used for the reduction of aldehydes are electron transfer reduction, hydride transfer reduction and hydrogenation reactions.[3] Both heterogeneous and homogeneous catalysts are used for these reductions. Particularly, transition metals such as Rh,[4] Ru,[5] Ir,[6] Pd,[7] Fe[8] and Au[9] catalyze hydrogenations using molecular hydrogen as reducing agent and represent the most preferred methods due to their reaction efficiency and minimal side reactions. Palladium on charcoal (Pd/C) is one of the significant catalysts in the catalytic hydrogenation reactions in the presence of molecular hydrogen.[10] The drawback of Pd/C are not only that it is expensive, highly flammable and difficult to recover and reuse, particularly for large scale reactions. The major disadvantages associated with the catalytic hydrogenation reaction are often the requirement of autoclaves, special equipment such as Parr equipment, high pressure,[11] usage of organic solvents such as ethanol, methanol and ethyl acetate.

Recently, metal nanoparticles (NPs) have received increasing attention as catalysts in the academic and industrial research.[12] Since metal NPs have a large surface area to volume ratio and are endowed with a large number of potentially active sites for the substrates, they exhibit higher catalytic activity than the traditional heterogeneous catalysts. At the same time, these metal NPs also retain the advantages of homogeneous catalyst, thus behaving as a semi-heterogeneous catalyst. The selectivity, stability and recyclability of the nanocatalysts are desperately dependent on the stabilizer and the solvent employed. Recently, there has been a great increase in the use of Pd NPs as catalyst in the hydrogenation reactions.[13] The majority of the methods used for the preparation of Pd NPs involve special solid supports and multistep stabilized preparation. Additionally, most of the methods used organic solvents.[14,15] The use of water rather than organic solvents is a growing demand in the chemical industry. Water is a cheap, non-hazardous, safe, eco-friendly and economically benign solvent. However, to the best of our knowledge, no palladium nanocatalyst has been explored for the hydrogenation of aldehydes in aqueous medium. As part of our ongoing research towards transition metal nanocatalysts,[16] we herein report a green and suitable strategy for the hydrogenation of aldehydes using a palladium nanocatalyst in water as the solvent (Scheme 1).

The initial study was carried out by treating 4-methylbenzaldehyde **1** with molecular hydrogen (H_2 balloon) as reducing agent in the presence of very stable Pd-BNP **4a** as catalyst in water (Figure 1) and the product **2a** was obtained in 83% (Table 1, entry 1). Encouraged by this initial result, we started the investigation of other Pd-NPs as catalyst stabilized by phenyl (**4b**) and 4-decylphenyl (**4c**)[16c] groups for this chemoselective hydrogenation of aromatic aldehydes and the results are summarized in Table 1 (entries 2 and 3). To further improve the yield of the reaction, different amounts of the Pd-BNP **4a** catalyst



Scheme 1. Approaches to the chemoselective hydrogenation of aldehydes.

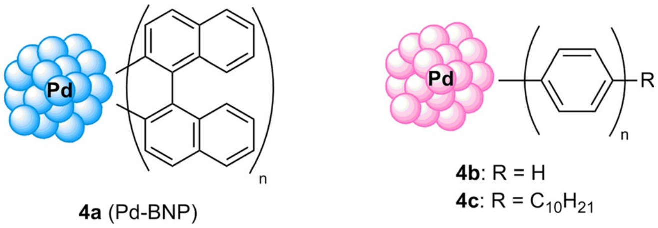
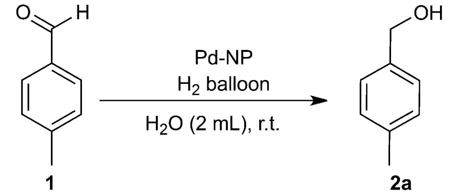


Figure 1. Aromatic derivative-stabilized Pd NPs.

Table 1. Screening of catalytic loading of Pd nanocatalyst for the hydrogenation of aldehydes.[a]



Entry	Pd-NP	Time [h]	Yield [%][b]
1	**4a** (0.5 mol%)	12	83
2	**4b** (0.5 mol%)	20	59
3	**4c** (0.5 mol%)	15	71
4	**4a** (1.0 mol%)	8	96
5	**4a** (1.5 mol%)	6	97
6	**4a** (2.0 mol%)	4	99
7	**4a** (2.5 mol%)	3	99
8	-	24	-

[a] *Reaction conditions:* 0.5 mmol of **1**.

[b] Isolated yield.

were screened. It is observed that 1 mol% of the catalyst afforded an excellent yield of 96% in 8 h (entry 4). Increasing the catalytic load increased the reaction rate with more or less the same yield. So, it is decided that 1 mol% of Pd-BNP **4a** will be used as optimized conditions (entry 4) as it gave a quantitative yield. It is important to mention that in the absence of Pd-BNP **4a**, no hydrogenation product was observed (entry 8).[18–20]

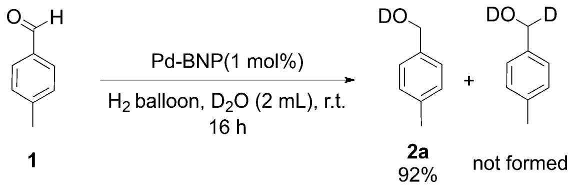
After achieving the best reaction conditions, the scope of the hydrogenation of various aldehydes was investigated and the results are summarized in Table 2. Aldehydes containing electron-releasing and electron-withdrawing groups on the aromatic ring were well tolerated and gave the corresponding alcohols in good to excellent yield (entries 3–18). Interestingly, highly labile halogen, cyano, acid, ester and keto group containing aldehydes also underwent this hydrogenation reaction smoothly and provided the corresponding alcohols in good yield (entries 8 and 12–16). Even *ortho*-substitution containing aldehydes gave the corresponding reduction products in good yields (entries 4 and 7).

When the reduction reaction was carried out with *para*- and *ortho*-substituted bromo-/chlorobenzaldehyde, product formation was not observed. Aliphatic aldehydes such as phenylacetaldehyde and cinnamaldehyde also remained unreactive in this hydrogenation reaction. When heteroaromatic aldehydes such as 2-pyridinecarboxaldehyde and furfural were used in the reduction reaction under the standard reaction conditions as well as with 4 mol% of Pd-BNP **4a**, not even a trace amount of product formation took place.

To check whether this is a heterogeneous reaction or the reaction is catalyzed by leached Pd from the nanocatalyst, the reduction reaction was carried out with 10 equivalents of Hg. The absence of product formation in this reaction showed that the Pd-BNP is a heterogeneous catalyst.[17]

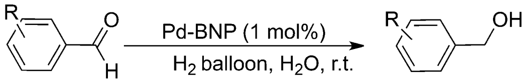
In a control experiment, we carried out the reaction with deuterium oxide (D_2O) as solvent and molecular hydrogen as reducing agent. Using D_2O as solvent, the reaction did not provide any deuterated alcohol **3a** (Scheme 2). With this experiment we conclude that the hydrogen source for the hydrogenation reaction is solely molecular hydrogen.

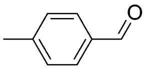
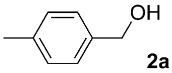
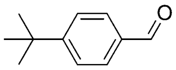
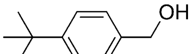
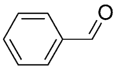
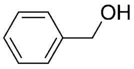
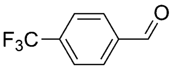
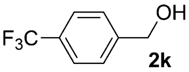
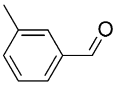
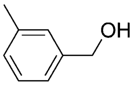
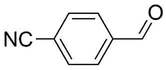
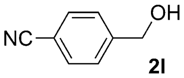
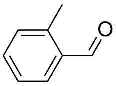
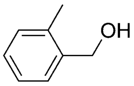
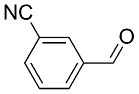
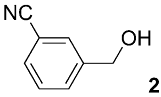
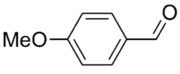
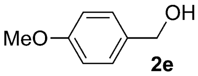
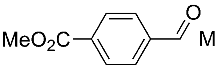
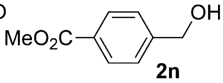
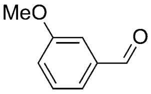
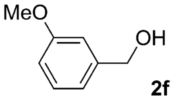
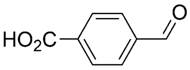
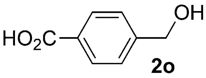
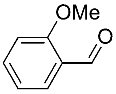
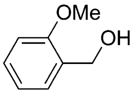
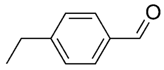
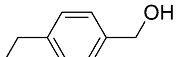
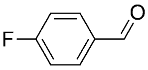
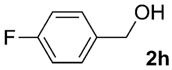
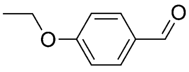
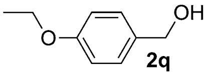
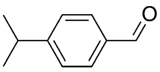
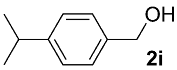
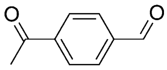
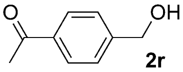
To study the scalability of this hydrogenation reaction of aldehydes in the presence Pd-BNP with molecular H_2, the reaction was performed in a gram scale in



Scheme 2. Reduction of **1** in D_2O.

Table 2. Substrate scope for alcohols with Pd-BNP catalyst.[a]



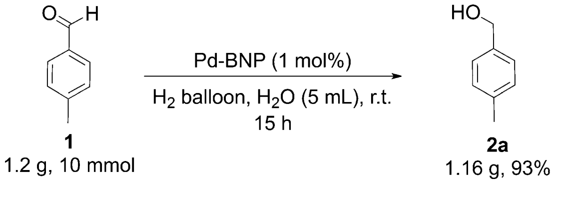
Entry	Aldehyde	Product	Time [h]	Yield [%][b]	Entry	Aldehyde	Product	Time [h]	Yield [%][b]
1		 **2a**	8	96	10		 **2j**	9	95
2		 **2b**	6	90	11		 **2k**	12	88
3		 **2c**	11	89	12		 **2l**	10	95
4		 **2d**	15	85	13		 **2m**	16	91
5		 **2e**	10	93	14		 **2n**	11	93
6		 **2f**	14	87	15		 **2o**	12	95
7		 **2g**	20	82	16		 **2p**	10	92
8		 **2h**	9	92	17		 **2q**	13	89
9		 **2i**	10	96	18		 **2r**	11	93

[a] *Reaction conditions:* aldehyde **1** (0.5 mmol), 5.3 mg Pd-BNP (10 wt% by ICP-OES analysis) in water (2 mL) at room temperature.

[b] Isolated yield.

water and the reaction gave a 93% isolated yield (Scheme 3).

After the successful utilization of stable Pd-BNP catalyst for the hydrogenation of aldehydes in water, the recoverability and recyclability of the nanocatalyst were investigated on hydrogenation of aldehydes. With completion of the hydrogenation of an aldehyde, the mother liquor was diluted with EtOH and centrifuged. The resulting solid was washed with ethanol and dried under vacuum. The recovered Pd nanocatalyst was used for further hydrogenation cycles. The Pd-BNP was successfully recovered and reused for five times without loss in catalytic activity (Figure 2).



Scheme 3. Gram scale reaction.

HR-TEM analysis of the recovered Pd-BNP showed that the recovered Pd-BNP had the same particle size without any apparent agglomeration even after the fifth catalytic cycle of the hydrogenation of an aldehyde (Figure 3).

In conclusion, we have developed an efficient, green and catalytic process for the hydrogenation of aldehydes. Particularly, cheap, non-flammable, non-toxic and eco-friendly water is used as a solvent. Hydrogenation with molecular hydrogen, water as a solvent and recyclability of the stable Pd-BNP nanocatalyst makes this methodology novel and environmentally benign.

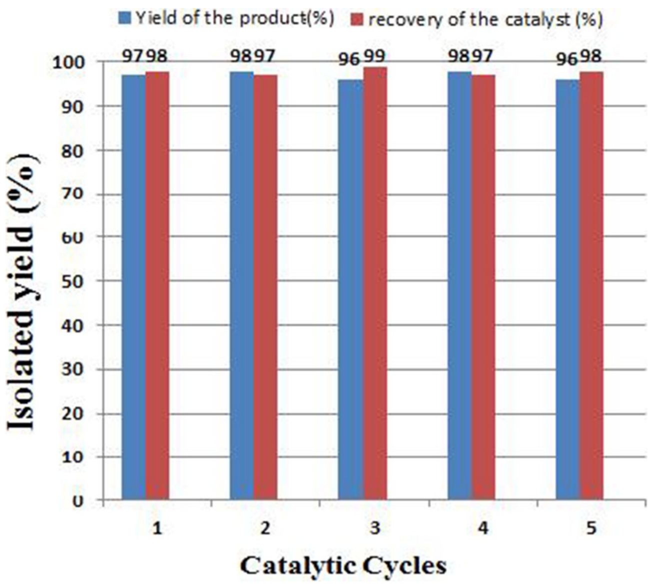


Figure 2. Catalytic recycles of Pd-BNP for the hydrogenation.

Experimental Section

Typical Experimental Procedure for Aldehyde Reduction (3)

Aldehyde (0.5 mmol), Pd-BNP (5.3 mg, 1.0 mol%) and water (2.0 mL) were charged in a reaction tube equipped with bar magnetic pellet. The resulting reaction mixture was stirred at room temperature under a hydrogen atmosphere (using H_2 balloon) and the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was extracted with ethyl acetate (2×20 mL). The organic layer was dried over $MgSO_4$ and concentrated under vacuum. The product was further purified by column chromatography using silica gel to afford the pure alcohol.

Acknowledgements

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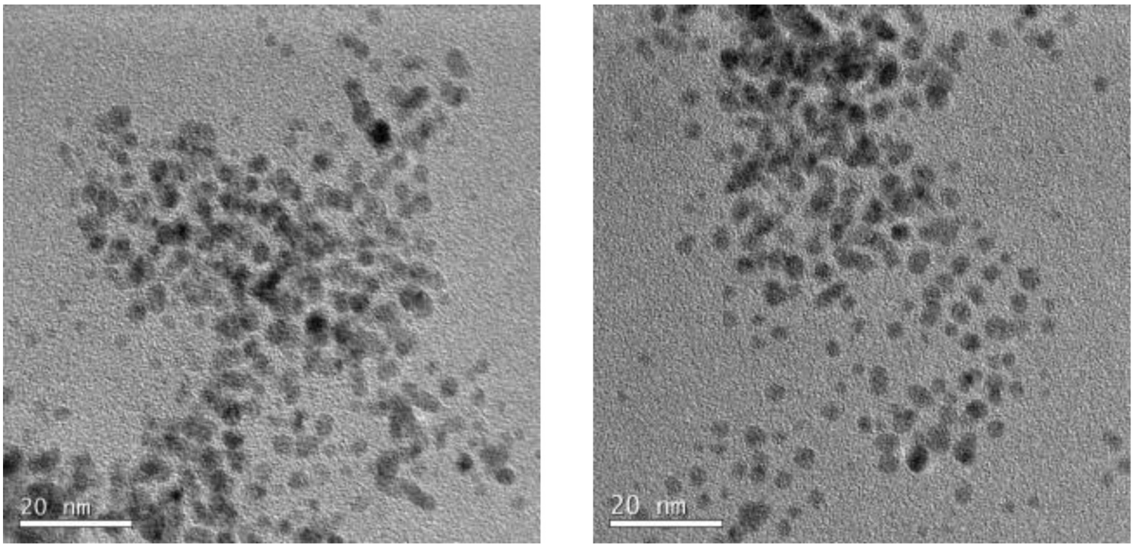

Figure 3. HR-TEM images of Pd-BNP catalyst before the first (*left*) and after the fifth catalytic cycle (*right*).

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[18] Pressure of a hydrogen balloon is **1** atm. We have also carried out three different reactions of 4-methylbenzaldehyde **1** (3 mmol) with 1 mol% of Pd-BNP in 5 mL water in a Shaker hydrogenator apparatus with 1 atm, 2 atm and 4 atm hydrogen pressure. The isolated yields of the product **2a** for all these cases are 93%, 94% and 97% with different reaction times. The reaction with 1 atm hydrogen pressure was completed within 17 h, but 2 atm and 4 atm hydrogen pressure reactions took 12 h and 5 h for completion. In higher atmospheric hydrogen pressures, reduction of the reaction time was observed. Increasing the H_2 pressure increases the rate of reaction without affecting the yield of the product.

[19] When the reduction reaction of 4-methylbenzaldehyde **1** with 1 mol% of catalyst was carried out with different lipophilic solvents such a carbon tetrachloride, benzene, toluene and hexanes, only 10–20% yields of the product **2a** were isolated after 24 h of reaction. These observations show that the rate of reaction is accelerated when water is used as solvent and reduction is more favorable in water than in the lipophilic solvents.

[20] We have performed the reduction reaction of 0.5 mmol of 4-methylbenzaldehyde **1** with 1 mL and 0.5 mL of water, 83% and 55% yields of alcohol **2a** were isolated. The yield of the product **2a** was decreased by increasing the concentration of the reaction.